

## II. REMARKS

### Formal Matters

Claims 1-27 are pending after entry of the amendments set forth herein.

Claims 1, 2, and 7-10 were examined and were rejected. Claims 3-6 and 11-23 were withdrawn from consideration.

Claims 1, 2, 7, and 10 are amended. The amendments to the claims were made solely in the interest of expediting prosecution, and are not to be construed as an acquiescence to any objection or rejection of any claim. Support for the amendments to claims 1, 2, 7, and 10 is found in the claims as originally filed, and throughout the specification, in particular at the following exemplary locations: claim 1: page 8, lines 15-24; claim 2: page 6, lines 12-16; and page 10, lines 14-16; claim 7: page 14, lines 21-23; claim 10: page 6, lines 12-16; and page 10, lines 14-19. Accordingly, no new matter is added by these amendments.

Claims 24-27 are added. Support for new claims 24-27 is found in the claims as originally filed, and throughout the specification, including the following exemplary locations: claim 24: page 8, lines 15-24; claim 25: page 6, lines 12-16; and page 10, lines 14-19; claim 26: page 11, lines 4-5; claim 27: page 12, lines 3-11. Accordingly, no new matter is added by these new claims.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

### Objection to the specification

The Office Action objected to the specification. The Office Action stated that (1) Figure 8A lists four sequences, the fourth of which has no associated SEQ ID NO either in the figure or in the description of the figure; and (2) Figure 10A shows a comparison of two amino acid sequences with no associated SEQ ID NOs.

Applicants respectfully request entry of the above-noted amendments to the specification to refer to the sequence identifiers.

### Claim objections

The Office Action stated that claims 1-3 and 7-10 are objected to.

Applicants note that claim 3 has been withdrawn from consideration.

Claim 2

The Office Action stated that claim 2 recites “DGAT2 $\alpha$ ” and suggested that this abbreviation be spelled out.

Applicants respectfully request entry of the above-noted amendment to claim 2, which spells out “DGAT2 $\alpha$ .”

Claim 7

The Office Action suggested placing a comma after the phrase “transcriptional initiation region”; and suggested changing “nucleic acid according to claim 1” to “polynucleotide according to claim 1.”

It is Applicants’ position that there is no need to insert a comma after “transcriptional initiation region.”

Applicants respectfully request entry of the amendment to claim 7 to recite “polynucleotide” instead of “nucleic acid.”

Claims 1-3 and 7-10

The Office Action stated claims 1-3 and 7-10 contain non-elected subject matter.

Applicants respectfully request entry of the above-noted amendment to claim 1, which amendment deletes reference to non-elected subject matter.

Rejection under 35 U.S.C. §112, second paragraph

Claim 2 was rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite.

The Office Action stated that the recitation of “DGAT2 $\alpha$ ” renders the claim indefinite, and stated that the specification fails to teach which identifying characteristics distinguish a DGAT2 $\alpha$  from other proteins. Applicants respectfully traverse the rejection.

Without conceding as to the correctness of this rejection, claim 2 is amended to recite “wherein the encoded polypeptide exhibits diacylglycerol acyltransferase activity.”

Applicants submit that the rejection of claim 2 under 35 U.S.C. §112, second paragraph, has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejection under 35 U.S.C. §112, first paragraph

Claims 1, 2, and 7-10 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement.

The Office Action stated that the specification does not reasonably provide enablement for any polynucleotide that encodes any polypeptide that exhibits diacylglycerol transferase activity wherein said polynucleotide has a mere 50% identity to SEQ ID NO:03. Applicants respectfully traverse the rejection.

The specification provides ample description of how to make and use a polynucleotide as recited in claim 1. The instant specification provides at least four polynucleotides that comprise a nucleotide sequence that encode a polypeptide that exhibits monoacylglycerol and/or diacylglycerol acyltransferase activity and that comprise a nucleotide sequence that has at least 50% nucleotide sequence identity to the sequence set forth in SEQ ID NO:03. For example, the instant specification provides SEQ ID NO:01, SEQ ID NO:03, SEQ ID NO:09, and SEQ ID NO:11. SEQ ID NOs:01, 09, and 11 share 90%, 89%, and 81% nucleotide sequence identity, respectively, with SEQ ID NO:03. SEQ ID NOs:01, 03, 09, and 11 encode polypeptides that exhibit monoacylglycerol and/or diacylglycerol acyltransferase activity. Furthermore, the specification provides a detailed description of how to measure monoacylglycerol and diacylglycerol acyltransferase activity. Specification, page 46, lines 11 to 28.

Nevertheless, and solely in the interest of expediting prosecution, claim 1 is amended to recite a polynucleotide that encodes a polypeptide that exhibits monoacylglycerol and/or diacylglycerol acyltransferase activity and that comprises a nucleotide sequence that has at least 90% nucleotide sequence identity to the sequence set forth in SEQ ID NO:03. The specification provides ample description of how to make and use a polynucleotide as recited in claim 1 as amended.

The law regarding enablement of inventions is clear: “[t]he test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.”<sup>1</sup>

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<sup>1</sup> *United States v. Electronics, Inc.*, 8 USPQ 2d 1217, 1233 (Fed. Cir. 1988), cert. denied, 490 U.S. 1046 (1989). See also *Genentech, Inc. v. Novo Nordisk*, 42 USPQ 2d 1001 (Fed. Cir. 1997), cert. denied, 522 U.S. 963 (1997); *Scripps Clinic and*

To aid in determinations of enablement, courts have identified eight factors for consideration: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability or unpredictability of the art; and (h) the breadth of the claims.<sup>2</sup>

The instant specification provides at least two polynucleotides that comprise a nucleotide sequence that encode a polypeptide that exhibits monoacylglycerol and/or diacylglycerol acyltransferase activity and that comprise a nucleotide sequence that has at least 90% nucleotide sequence identity to the sequence set forth in SEQ ID NO:03. For example, the instant specification provides SEQ ID NO:01 and SEQ ID NO:03. SEQ ID NO:01 and SEQ ID NO:03 share 90% nucleotide sequence identity, and encode polypeptides that exhibit monoacylglycerol and/or diacylglycerol acyltransferase activity. Furthermore, the specification provides a detailed description of how to measure monoacylglycerol and diacylglycerol acyltransferase activity. Specification, page 46, lines 11 to 28.

Applicants respectfully submit that the specification and the amended claims, coupled with the information known in the art, would enable one of skill in the art to use the invention without undue experimentation. Relevant enablement factors are discussed in detail below.

**(a) the quantity of experimentation necessary:**

The courts have clearly taught that the fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. For example, see MPEP §2164.01.<sup>3</sup>

As the court explained<sup>4</sup>:

“[A] considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.”

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*Research Foundation v. Genentech, Inc.*, 18 USPQ 2d 1001 (Fed. Cir. 1991).

<sup>2</sup> *Ex Parte Forman*, 230 USPQ 546, 547 (Bd.Pat.App & Interf. 1986); and, *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

<sup>3</sup> See also *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd sub nom.*, *Massachusetts Institute of Technology v. A.B. Fortia*, 227 USPQ 428 (Fed. Cir. 1985).

<sup>4</sup> *In re Wands* 8 USPQ 2d at 1404

Practitioners in the chemical and molecular biology arts frequently engage in extensive modification of reaction conditions and complex and lengthy experimentation where many factors must be varied to succeed in performing an experiment or in producing a desired result. The Federal Circuit has found that such extensive experimentation is not undue in the molecular biology arts. For example, the court concluded that extensive screening experiments, while being voluminous, were not undue in view of the art which routinely performs such long experiments.<sup>5</sup>

Claim 1 as amended recites a polynucleotide that encodes a polypeptide that exhibits monoacylglycerol and/or diacylglycerol acyltransferase activity and comprises a nucleotide sequence that has at least 90% nucleotide sequence identity to the sequence set forth in SEQ ID NO:03. The only experiments, if any, that need be performed to enable the entire scope of the claim are those designed to determine which sequences encode polypeptides that exhibit monoacylglycerol and/or diacylglycerol acyltransferase activity. The sequence of polypeptides that exhibit monoacylglycerol and/or diacylglycerol acyltransferase activity is determined through routine experimentation, typically employing nothing more than performing the same assay disclosed in the specification on a variety of sequence variants of the polypeptide made by routine recombinant DNA techniques. Since these experiments routine in nature, no undue experimentation is required. In other words, the only experimentation that may be required to enable the claimed invention are those experiments to determine the presence of a certain activity, and since this only requires a routine assay on polypeptide variants to determine the active variants, no undue experimentation is necessary.

**(b) the amount of direction or guidance presented**

As noted above, the instant specification provides at least two polynucleotides that comprise a nucleotide sequence that encode a polypeptide that exhibits monoacylglycerol and/or diacylglycerol acyltransferase activity and that comprise a nucleotide sequence that has at least 90% nucleotide sequence identity to the sequence set forth in SEQ ID NO:03. For example, the instant specification provides SEQ ID NO:01 and SEQ ID NO:03. SEQ ID NO:01 and SEQ ID NO:03 share 90% nucleotide sequence identity, and encode polypeptides that exhibit monoacylglycerol and/or diacylglycerol acyltransferase activity. Furthermore, the specification provides a detailed description of how to

measure monoacylglycerol and diacylglycerol acyltransferase activity. Specification, page 46, lines 11 to 28.

**(c) the presence or absence of working examples:**

Compliance with the enablement requirement under Section 35 U.S.C. §112, first paragraph does not require or mandate that a specific example be disclosed. The specification need not contain a working example if the invention is otherwise disclosed in such a manner that one skilled in the art would be able to practice the invention without undue experimentation.<sup>6</sup> Furthermore, “Nothing more than objective enablement is required, and therefore it is irrelevant whether [a] teaching is provided through broad terminology or illustrative examples.”<sup>7</sup>

**(f) the relative skill of those in the art:**

The relevant ordinarily skilled artisan is generally a skilled laboratory technician with experience in molecular biology and/or a scientist with the equivalent of a doctoral degree in molecular biology techniques. Furthermore, such artisans are required to keep abreast of the latest technology through continuing education and reading of scientific journal articles. As such, the skill level of those developing and using methods for manipulating DNA and performing enzyme assays is high.

**(g) the predictability or unpredictability of the art**

In making this rejection, the Examiner asserts that the relationship between the sequence of a peptide and its tertiary structure are not well understood and are not predictable.

However, the courts have clearly taught that even in unpredictable arts the specification does not have to disclose every species of a genus that would work and every species that would not work.

The court has very clearly explained<sup>8</sup>:

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<sup>5</sup> *Hybritech v. Monoclonal Antibodies, Inc.* 231 USPQ 81 (Fed. Cir. 1986)

<sup>6</sup> *In re Borkowski*, 164 USPQ at 645.

<sup>7</sup> *In re Robins* 166 USPQ 552 at 555 (CCPA 1970).

<sup>8</sup> *In re Angstadt*, 190 USPQ at 218.



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USSN: 10/046,924

"To require such a complete disclosure would apparently necessitate a patent application or applications with thousands of catalysts....More importantly, such a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments. This would tend to discourage inventors from filing patent applications in an unpredictable area since the patent claims would have to be limited to those embodiments which are expressly disclosed. A potential infringer could readily avoid literal infringement of such claims by merely finding another analogous catalyst complex which could be used ...."

Claim 1 recites a polynucleotide that encodes a polypeptide that exhibits monoacylglycerol and/or diacylglycerol acyltransferase activity and comprises a nucleotide sequence that has at least 90% nucleotide sequence identity to the sequence set forth in SEQ ID NO:03. Since one of skill in the art would recognize that a reasonable correlation exists between the activities of polypeptides in this genus, and since every species in a genus does not have to be tested for a genus to be enabled, extensive disclosure or guidance of the active species of a genus does not have to be provided for a genus of this scope to be enabled.

#### **(h) the breadth of the claims**

Claim 1 as amended recites a polynucleotide that encodes a polypeptide that exhibits monoacylglycerol and/or diacylglycerol acyltransferase activity and comprises a nucleotide sequence that has at least 90% nucleotide sequence identity to the sequence set forth in SEQ ID NO:03. In other words, in order to fall within a claim, an encoded polypeptide must exhibit monoacylglycerol and/or diacylglycerol acyltransferase activity. *Thus, the claim language excludes polynucleotides encoding polypeptides that do not exhibit this activity.*

In sum, the amount of experimentation required to identify polynucleotides that encode a polypeptide that exhibits monoacylglycerol and/or diacylglycerol acyltransferase activity and that comprise a nucleotide sequence that has at least 90% nucleotide sequence identity to the sequence set forth in SEQ ID NO:03 would not be undue because a) a working example has been provided, b) guidance is given on how to test the encoded polypeptide has been provided, c) there is a good correlation between the activities of species within a genus of this breadth, and d) one of skill in the art would be able to perform the experiments as a matter of routine to determine the active sequences.

The specification therefore provides sufficient enablement such that one of ordinary skill in the art would be able to practice the invention without undue experimentation.

Applicants submit that the rejection of claims 1, 2, and 7-10 under 35 U.S.C. §112, first paragraph, has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejection under 35 U.S.C. §102(a)

Claims 1, 2, and 7-10 were rejected under 35 U.S.C. §102(a) as allegedly anticipated by Baker et al. (WO 00/12708; “Baker”).

The Office Action stated that Baker teaches a polynucleotide shown in Figure 164 of Baker, which is “greater than 89% identical” over the entire length of instantly disclosed SEQ ID NO:03. Office Action, page 10. The Office Action stated that Baker anticipates claim 1.

Baker does not teach a polynucleotide which is greater than 89% over the entire length of SEQ ID NO:3. An alignment of the sequence of Figure 164 of Baker with SEQ ID NO:03 indicates that the two sequences share no more than 89% sequence identity.

Claim 1 as amended recites a polynucleotide comprising a nucleotide sequence having at least 90% nucleotide sequence identity to SEQ ID NO:03. Accordingly, Baker cannot anticipate claim 1, nor can Baker anticipate claims 2 and 7-10 which depend, directly or indirectly, from claim 1.

Applicants submit that the rejection of claims 1, 2, and 7-10 under 35 U.S.C. §102(a) has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejection under 35 U.S.C. §102(b)

Claims 1, 2, and 7-10 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Specht et al. (WO 99/47655; “Specht”).

The Office Action stated that Specht teaches Sequence 21, which is 90% identical from nucleotide 548 through 1167 of SEQ ID NO:03, and which is 100% identical from nucleotide 552 through 1231 of SEQ ID NO:01. The Office Action stated that Specht does not teach that the disclosed polynucleotide encodes a “DGAT2 $\alpha$  product,” and that based on the extremely high sequence identity (100%) to SEQ ID NO:1, the polynucleotide taught by Specht inherently encodes a DGAT2 $\alpha$

polypeptide. Applicants respectfully traverse the rejection.

Applicants note that, in response to the Restriction Requirement dated April 24, 2003 in the instant case, Applicants elected Group I claims, and SEQ ID NO:03 for prosecution on the merits. Accordingly, Applicants' election renders comments made in the Office Action relating to SEQ ID NO:01 moot.

The Office Action stated that Specht teaches Sequence 21, which is 90% identical from nucleotide 548 through 1167 of SEQ ID NO:03. The instant specification states that DGAT2 $\alpha$  polypeptides range in length from about 300 to about 500 amino acids. Specification, page 7, lines 23-29. Sequence 21 of Specht could encode a polypeptide of at most about 227 amino acids. Sequence 21 of Specht does not encode a polypeptide that exhibits monoacylglycerol transferase and/or diacylglycerol transferase. Accordingly Specht cannot anticipate the instant invention as claimed.

Applicants submit that the rejection of claims 1, 2, and 7-10 under 35 U.S.C. §102(b) has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

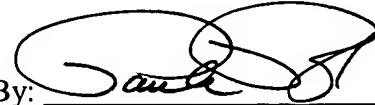
### III. CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number UCAL240CIP.

Respectfully submitted,  
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Date: Nov. 12, 2003

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